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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/578,355

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Robert C. Leif

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09/29/2010

THE NATH LAW GROUP

112 South West Street

Alexandria, VA 22314

EXAMINER

PERREIRA, MELISSA JEAN

ART UNIT

PAPER NUMBER

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DELIVERY MODE

09/29/2010

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/578,355	<b>Applicant(s)</b> LEIF ET AL.	
	<b>Examiner</b> MELISSA PERREIRA	<b>Art Unit</b> 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 09 August 2010.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-6,8,9 and 11-18 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6,8,9 and 11-18 is/are rejected.
- 7) ☒ Claim(s) 10 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Claims 1-6 and 8-18 are pending in the application. Claim 7 was canceled in the amendment filed 8/9/10. Any objections and/or rejections from previous office actions that have not been reiterated in this office action are obviated.

#### ***New Grounds of Rejection Necessitated by the Amendment***

##### ***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-6 and 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The recitation of, "said fluorophore and lumiphore are not a ligand of yttrium or a 3-valent lanthanide element having atomic number 59-71" and "the fluorophore or lumiphore energy transfer donor compound is not a complex of gadolinium (III)" in the instant claims is not supported in the specification to show applicant envisioned the invention commensurate in scope with these claims. Applicant does not point to the location in the specification that provides support for the limitation of "said fluorophore and lumiphore are not a ligand of yttrium or

Art Unit: 1618

a 3-valent lanthanide element having atomic number 59-71" and "the fluorophore or lumiphore energy transfer donor compound is not a complex of gadolinium (III)."

3. The specification states that, "the term lanthanide is used to designate any of the lanthanide elements (atomic number 57-71) as well as the lanthanide-like yttrium and the actinide elements (atomic number 89-103) (specification, p1, lines 4-6) and "these ligands are characterized by electron donating atoms, such as oxygen, nitrogen sulfur or phosphorus, and are able to coordinate with the energy acceptor lanthanide(III) or with energy donor gadolinium (III) or yttrium (III) ions" (specification, p41, lines 8-11). The specification further states that, "M is a metal ion selected from the group consisting of a lanthanide having atomic number 57-71, an actinide atomic number 89-103, and yttrium having atomic number 39" (specification, p31, lines 26-31; p32, lines 24-31) and "these fluorophore and/or lumiphore donor metal ions are selected from the group of Gd(III), Y(III), etc." (specification, p42, lines 17-21). The mere absence of a positive recitation is not a basis for an exclusion. See MPEP 2100-228

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claim 4 is confusing as it recites, "M is a metal ion selected from the group consisting of a lanthanide having atomic number 57-71 an actinide having atomic number 89-103 and yttrium (III) having atomic number 39"

Art Unit: 1618

wherein the instant claim 1, to which claim 4 depends, states that the fluorophore and lumiphore are not a ligand of yttrium or a 3-valent lanthanide element having atomic number 59-71.

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

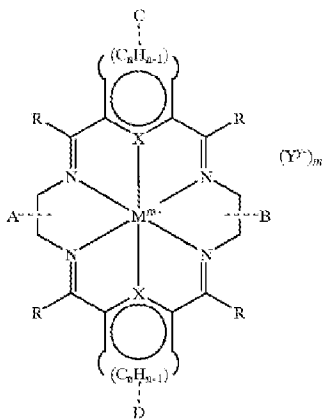
7. Claims 1-4,6,16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Leif et al. (US 6,340,744 B1).

8. Leif et al. (US 6,340,744 B1) teaches of spectrofluorimetrically detectable luminescent compositions comprising a.) at least one energy transfer acceptor lanthanide element macrocycle compound which may be substituted with reactive functional groups at which reaction with analytes can take place (analyte binding species) and has an emission spectrum peak in the range from 500-950 nm; b.) at least one energy transfer donor compound (abstract; claim 1, column 2, lines 16+; column 8, lines 7-22; column 9, lines 45+; column 10, lines 1-13; column 11, lines 60+). The enhanced luminescence afforded by the composition enables the detection and/or quantitation of many analytes in low concentration without the use of expensive, complicated time-gated detection systems (abstract). The luminescent compositions of

Art Unit: 1618

the disclosure are combined with a sample containing an analyte in an aqueous solution (column 11, lines 33-45).

9. The energy transfer acceptor macrocyclic compound has the formula (below) wherein M is a metal ion selected from the group consisting of an actinide having atomic number 89-103, etc. that does not include yttrium or gadolinium; R is hydrogen, straight-chain alkyl, etc.; X is selected from the group consisting of nitrogen, sulfur and oxygen which forms a part of a ring structure selected from the group consisting of pyridine, etc.; n is 2 or 3; Y is a negatively charged ion; m is the ionic charge of the metal ion in the macrocyclic complex;  $y^-$  is the ionic charge of the counterion in the macrocyclic complex; A,B,C and D are selected substituents selected from the group consisting of hydrogen, straight-chain alkyl, etc. (claim 1; column 2, lines 17-27; column 4).



10.

11. The luminescent compositions of the disclosure emit energy (enhanced luminescence in the range of 500-950 nm) upon excitation in the range of 200-400 nm (column 3, lines 8-12 and 55-60). The luminescent compositions of the disclosure may further comprise a micelle-producing amount of at least one surfactant and may be

Art Unit: 1618

lyophilized to form a solid after transfer to an immiscible non-aqueous medium (column 2, lines 16-28; column 10, lines 21-34).

12. Also, the intended use, such as unitary luminescence enhancing solution is not generally afforded any patentable weight and since the combination leads to the same compounds as claimed, they would be expected to be capable of performing the same intended use. "The recitation of a new intended use for an old product does not make a claim to that old product patentable." *In re Schreiber*, 44 USPQ2d 1429 (Fed. Cir. 1997).

### ***Response to Arguments***

13. Applicant's arguments filed 8/9/10 have been fully considered but they are not persuasive.

14. Applicant asserts that claim 1 has been amended to provide that the fluorophore and lumiphore (the energy transfer donor) are not a ligand of yttrium or a 3-valent lanthanide element having atomic number 59-71. The '744 patent requires that the energy transfer donor be one of a compound of yttrium or a 3-valent lanthanide element having atomic number 59-71.

15. Leif et al. teaches that the energy transfer acceptor macrocyclic compound has the formula (above) wherein M is a metal ion selected from the group consisting of an actinide having atomic number 89-103, etc. that does not include yttrium or gadolinium. Therefore, the fluorophore and lumiphore (the energy transfer donor) are not a ligand of yttrium or a 3-valent lanthanide element having atomic number 59-71 but is a ligand of an actinide having atomic number 89-103.

Art Unit: 1618

16. Claims 8,9,11 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Leif et al. (US 6,340,744 B1).

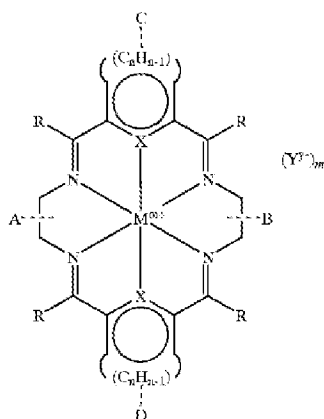
17. Leif et al. (US 6,340,744 B1) teaches of spectrofluorimetrically detectable luminescent compositions comprising a.) at least one energy transfer acceptor lanthanide element macrocycle compound which may be substituted with reactive functional groups at which reaction with analytes can take place (analyte binding species) and has an emission spectrum peak in the range from 500-950 nm; b.) at least one energy transfer donor compound (i.e. 3-valent lanthanide element having an atomic number 59-71, ionic compound of or complex of gadolinium (III)), provided that the lanthanide element of the macrocycle and donor are not identical (abstract; claim 1, column 2, lines 16+; column 8, lines 7-22; column 9, lines 45+; column 10, lines 1-13; column 11, lines 60+). The enhanced luminescence afforded by the composition enables the detection and/or quantitation of many analytes in low concentration without the use of expensive, complicated time-gated detection systems (abstract). The luminescent compositions of the disclosure are combined with a sample containing an analyte in an aqueous solution (column 11, lines 33-45).

18. The lanthanide energy transfer acceptor macrocyclic compound has the formula (below) wherein M is a metal ion selected from the group consisting of a lanthanide having an atomic number 59-71, an actinide having atomic number 89-103, etc.; R is hydrogen, straight-chain alkyl, etc.; X is selected from the group consisting of nitrogen, sulfur and oxygen which forms a part of a ring structure selected from the group consisting of pyridine, etc.; n is 2 or 3; Y is a negatively charged ion; m is the ionic



Art Unit: 1618

charge of the metal ion in the macrocyclic complex;  $y^-$  is the ionic charge of the counterion in the macrocyclic complex; A,B,C and D are selected substituents selected from the group consisting of hydrogen, straight-chain alkyl, etc. (claim 1; column 2, lines 17-27; column 4).



19.

20. The luminescent compositions of the disclosure emit energy (enhanced luminescence in the range of 500-950 nm) upon excitation in the range of 200-400 nm (column 3, lines 8-12 and 55-60). The luminescent compositions of the disclosure may further comprise a micelle-producing amount of at least one surfactant and may be lyophilized to form a solid after transfer to an immiscible non-aqueous medium (column 2, lines 16-28; column 10, lines 21-34).

21. It is respectfully pointed out that instant claims 8,9,11 and 12 are product-by-process limitations. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different

Art Unit: 1618

process. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed Cir. 1985). See MPEP 2113.

22. Also, the intended use, such as unitary luminescence enhancing solution is not generally afforded any patentable weight and since the combination leads to the same compounds as claimed, they would be expected to be capable of performing the same intended use. "The recitation of a new intended use for an old product does not make a claim to that old product patentable." *In re Schreiber*, 44 USPQ2d 1429 (Fed. Cir. 1997).

### ***Response to Arguments***

23. Applicant's arguments filed 8/9/10 have been fully considered but they are not persuasive.

24. Applicant asserts that claims 8-13 are not product-by-process claims and are directed to a composition having certain properties.

25. The instant claim 8 recites, "that after drying results in a solid that enhances the luminescence of an energy transfer acceptor lanthanide ion complex by a mechanism other than completing the complexation of the lanthanide ions" which is a product-by-process limitation as the product of the instant claims does not depend on the method of its production.

### ***Claim Rejections - 35 USC § 103***

26. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

Art Unit: 1618

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

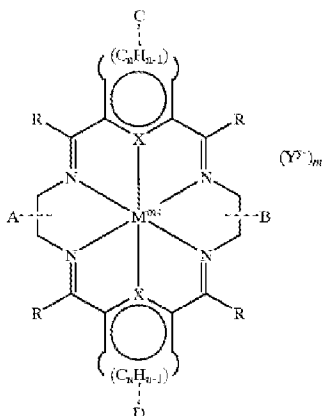
27. Claims 1-6, 16 and 17 rejected under 35 U.S.C. 103(a) as being unpatentable over Leif et al. (US 6,340,744 B1) in view of Mathis et al. (US 4,927,923).

28. Leif et al. (US 6,340,744 B1) teaches of spectrofluorimetrically detectable luminescent compositions comprising a.) at least one energy transfer acceptor lanthanide element macrocycle compound which may be substituted with reactive functional groups at which reaction with analytes can take place (analyte binding species) and has an emission spectrum peak in the range from 500-950 nm; b.) at least one energy transfer donor compound (abstract; claim 1, column 2, lines 16+; column 8, lines 7-22; column 9, lines 45+; column 10, lines 1-13; column 11, lines 60+). The enhanced luminescence afforded by the composition enables the detection and/or quantitation of many analytes in low concentration without the use of expensive, complicated time-gated detection systems (abstract). The luminescent compositions of the disclosure are combined with a sample containing an analyte in an aqueous solution (column 11, lines 33-45).

29. The energy transfer acceptor macrocyclic compound has the formula (below) wherein M is a metal ion selected from the group consisting of an actinide having atomic number 89-103, etc. that does not include yttrium or gadolinium; R is hydrogen, straight-chain alkyl, etc.; X is selected from the group consisting of nitrogen, sulfur and oxygen which forms a part of a ring structure selected from the group consisting of pyridine, etc.; n is 2 or 3; Y is a negatively charged ion; m is the ionic charge of the metal ion in the macrocyclic complex; y<sup>-</sup> is the ionic charge of the counterion in the macrocyclic

Art Unit: 1618

complex; A,B,C and D are selected substituents selected from the group consisting of hydrogen, straight-chain alkyl, etc. (claim 1; column 2, lines 17-27; column 4).



30.

31. The luminescent compositions of the disclosure emit energy (enhanced luminescence in the range of 500-950 nm) upon excitation in the range of 200-400 nm (column 3, lines 8-12 and 55-60). The luminescent compositions of the disclosure may further comprise a micelle-producing amount of at least one surfactant and may be lyophilized to form a solid after transfer to an immiscible non-aqueous medium (column 2, lines 16-28; column 10, lines 21-34).

32. Leif et al. does not disclose a cryptate.

33. Mathis et al. (US 4,927,923) discloses macropolycyclic rare earth complexes, namely cryptates which are useful as fluorescent tracers for biological substances in immunological detection or determination techniques using fluorescence. The excitation of the cryptate rare earth complexes enhances the fluorescence characteristics of a rare earth ion as excitation of an isolated rare earth ion produces only a very weak fluorescence because they generally have low molar absorption coefficients  $\epsilon$  (abstract; column 3, lines +; column 4, lines 1-37).

Art Unit: 1618

34. At the time of the invention one ordinarily skilled in the art to substitute the cryptate of Mathis et al. for the macrocyclic chelator of Leif et al. to examine the enhancement of the fluorescence of the luminescent compositions for determination techniques as excitation of the cryptate rare earth complexes enhances the fluorescence characteristics of a rare earth ion which generally have low molar absorption coefficients e.

35. It is obvious to those skilled in the art to make known substitutions on compounds that are similar in structure and function to observe the effects on the function of such compounds and to use the observations/data to further manipulate a compound to generate the desired effect, such as the enhancement of the fluorescence of the luminescent compositions for use in the detection and/or quantitation of many analytes in low concentration without the use of expensive, complicated time-gated detection systems.

### ***Response to Arguments***

36. Applicant's arguments filed 8/9/10 have been fully considered but they are not persuasive.

37. Applicant asserts that claim 1 has been amended to provide that the fluorophore and lumiphore (the energy transfer donor) are not a ligand of yttrium or a 3-valent lanthanide element having atomic number 59-71. The '744 patent requires that the energy transfer donor be one of a compound of yttrium or a 3-valent lanthanide element having atomic number 59-71.

Art Unit: 1618

38. Leif et al. teaches that the energy transfer acceptor macrocyclic compound has the formula (above) wherein M is a metal ion selected from the group consisting of an actinide having atomic number 89-103, etc. that does not include yttrium or gadolinium. Therefore, the fluorophore and lumiphore (the energy transfer donor) are not a ligand of yttrium or a 3-valent lanthanide element having atomic number 59-71 but is a ligand of an actinide having atomic number 89-103.

39. Applicant asserts that the reference of Mathis et al. does not disclose, suggest, use of a cryptate with the compounds of the present invention as part of an energy transfer acceptor lanthanide ion complex. The compounds disclosed by Mathis et al. and the chemistry of those compounds, is not the same as that of the present macrocyclic compounds. There is nothing in Mathis et al. that would lead one of ordinary skill in the art to substitute the cryptate of Mathis et al. for the macrocyclic chelator of the present invention.

40. Mathis et al. was not used to teach of the compounds of the instant claims but was used to teach that cryptates are useful as fluorescent tracers for biological substances in immunological detection or determination techniques using fluorescence. The excitation of the cryptate rare earth complexes enhances the fluorescence characteristics of a rare earth ion as excitation of an isolated rare earth ion produces only a very weak fluorescence because they generally have low molar absorption coefficients e.

41. At the time of the invention one ordinarily skilled in the art to substitute the cryptate of Mathis et al. for the macrocyclic chelator of Leif et al. to examine the

Art Unit: 1618

enhancement of the fluorescence of the luminescent compositions for determination techniques as excitation of the cryptate rare earth complexes enhances the fluorescence characteristics of a rare earth ion which generally have low molar absorption coefficients e.

42. It is obvious to those skilled in the art to make known substitutions on compounds that are similar in structure and function to observe the effects on the function of such compounds and to use the observations/data to further manipulate a compound to generate the desired effect, such as the enhancement of the fluorescence of the luminescent compositions for use in the detection and/or quantitation of many analytes in low concentration without the use of expensive, complicated time-gated detection systems.

43. Claims 8,9,11,12-15 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leif et al. (US 6,340,744 B1) in view of Mathis et al. (US 4,927,923) and in further view of Vallarino et al. (US 5,696,240).

44. Leif et al. (US 6,340,744 B1) teaches of spectrofluorimetrically detectable luminescent compositions comprising a.) at least one energy transfer acceptor lanthanide element macrocycle compound which may be substituted with reactive functional groups at which reaction with analytes can take place (analyte binding species) and has an emission spectrum peak in the range from 500-950 nm; b.) at least one energy transfer donor compound (i.e. 3-valent lanthanide element having an atomic number 59-71, ionic compound of or complex of gadolinium (III)), provided that the

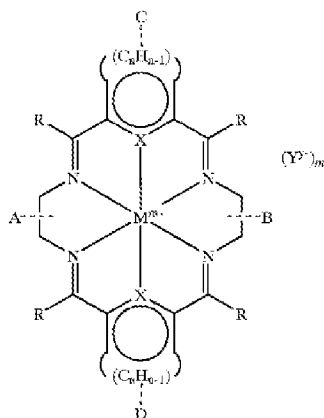
Art Unit: 1618

lanthanide element of the macrocycle and donor are not identical (abstract; claim 1, column 2, lines 16+; column 8, lines 7-22; column 9, lines 45+; column 10, lines 1-13; column 11, lines 60+). The enhanced luminescence afforded by the composition enables the detection and/or quantitation of many analytes in low concentration without the use of expensive, complicated time-gated detection systems (abstract). The luminescent compositions of the disclosure are combined with a sample containing an analyte in an aqueous solution (column 11, lines 33-45).

45. The lanthanide energy transfer acceptor macrocyclic compound has the formula (below) wherein M is a metal ion selected from the group consisting of a lanthanide having an atomic number 59-71, an actinide having atomic number 89-103, etc.; R is hydrogen, straight-chain alkyl, etc.; X is selected from the group consisting of nitrogen, sulfur and oxygen which forms a part of a ring structure selected from the group consisting of pyridine, etc.; n is 2 or 3; Y is a negatively charged ion; m is the ionic charge of the metal ion in the macrocyclic complex;  $y^-$  is the ionic charge of the counterion in the macrocyclic complex; A,B,C and D are selected substituents selected from the group consisting of hydrogen, straight-chain alkyl, etc. (claim 1; column 2, lines 17-27; column 4).



Art Unit: 1618



46.

47. The luminescent compositions of the disclosure emit energy (enhanced luminescence in the range of 500-950 nm) upon excitation in the range of 200-400 nm (column 3, lines 8-12 and 55-60). The luminescent compositions of the disclosure may further comprise a micelle-producing amount of at least one surfactant and may be lyophilized to form a solid after transfer to an immiscible non-aqueous medium (column 2, lines 16-28; column 10, lines 21-34).

48. Leif et al. further disclose the concentration range of the energy transfer donor species is in the range from  $1 \times 10^{-5}$  to  $1 \times 10^{-3}$  moles per liter (column 10, lines 4-8) which encompasses the concentration range of the energy transfer donor of the instant claims.

49. Leif et al. does not disclose a cryptate.

50. Mathis et al. (US 4,927,923) discloses macropolycyclic rare earth complexes, namely cryptates which are useful as fluorescent tracers for biological substances in immunological detection or determination techniques using fluorescence. The excitation of the cryptate rare earth complexes enhances the fluorescence characteristics of a rare earth ion as excitation of an isolated rare earth ion produces

Art Unit: 1618

only a very weak fluorescence because they generally have low molar absorption coefficients  $\epsilon$  (abstract; column 3, lines +; column 4, lines 1-37).

51. At the time of the invention one ordinarily skilled in the art to substitute the cryptate of Mathis et al. for the macrocyclic chelator of Leif et al. to examine the enhancement of the fluorescence of the luminescent compositions for determination techniques as excitation of the cryptate rare earth complexes enhances the fluorescence characteristics of a rare earth ion which generally have low molar absorption coefficients  $\epsilon$ .

52. It is obvious to those skilled in the art to make known substitutions on compounds that are similar in structure and function to observe the effects on the function of such compounds and to use the observations/data to further manipulate a compound to generate the desired effect, such as the enhancement of the fluorescence of the luminescent compositions for use in the detection and/or quantitation of many analytes in low concentration without the use of expensive, complicated time-gated detection systems.

53. In regards to claims 14 and 15:

54. Leif et al. discloses a method for analysis of a sample suspected of containing at least one analyte, frequently a biologically active compound comprising a.) contacting said sample with a functionalized complex of a metal in a reaction medium under binding conditions, wherein the reaction medium in which a sample containing or suspected of containing an analyte is an aqueous solution; b.) adding a luminescence-

Art Unit: 1618

enhancing amount of at least one energy transfer donor compound; c.) subjecting the reaction medium to excitation energy in the range of 200-400 nm, whereby enhanced luminescence in the range of 500-950 nm is generated; d.) (column 2, lines 28-36 and 53+; column 3, lines 1-19; column 11, lines 33-45); e.) monitoring said luminescence of the reaction medium to measure in said sample at least one of the following: (1) presence and/or concentration of said conjugate; (2) presence and/or concentration of the product of the interaction of said complex with said binding material (analyte); (3) presence and/or concentration of the product of the interaction of the conjugate with the binding material (analyte) (column 3, lines 1-20). The enhanced fluorescence composition of the invention formed in an aqueous micellar organization can be dried and/or transferred into an aqueous medium and measured in the non-aqueous environment or in the dry state (column 15, lines 13-17).

55. Leif et al. further discloses the preparation of EuMac-Avidin/biotinylated agarose beads via the procedures of US 5,696,240. The EuMac-Avidin/biotinylated agarose beads are treated with Gd(III) optimized cofluorescence matrix solution, were incubated, centrifuged and the solvent removed to generate dry beads. The beads were irradiated at 360 nm (example VIII).

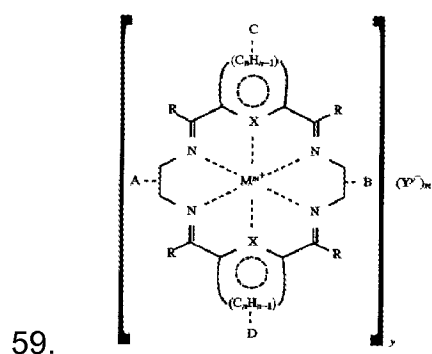
56. Leif et al. does not explicitly disclose all the method step of the instant claim 15.

57. Vallarino et al. (US 5,696,240) discloses macrocyclic complexes (below) which encompass the luminescent compositions of Leif et al., wherein M is a metal ion selected from the group consisting of a lanthanide having an atomic number 59-71, an actinide having atomic number 89-103, etc.; R is hydrogen, straight-chain alkyl, etc.; X

Art Unit: 1618

is selected from the group consisting of nitrogen, sulfur and oxygen which forms a part of a ring structure selected from the group consisting of pyridine, etc.;  $n$  is 2 or 3;  $Y$  is a negatively charged ion;  $m$  is the ionic charge of the metal ion in the macrocyclic complex;  $y^-$  is the ionic charge of the counterion in the macrocyclic complex; A,B,C and D are selected substituents selected from the group consisting of hydrogen, straight-chain alkyl, etc. (column 8, lines 32+; column 11, lines 1+; claim 4).

58. Vallarino et al. further discloses of the coupling of europium-macrocyclic complexes to agarose beads wherein the biotinylated agarose beads are washed and treated/incubated with the europium-macrocyclic-coupled avidin solution and then centrifuged and washed thoroughly (example XXIX, especially step 3).



60. At the time of the invention it would have been obvious to one ordinarily skilled in the art to use the solid support (agarose bead) preparation method of Vallarino et al. US 5,696,240 for the europium-macrocyclic-complexes of Leif et al. as Leif et al. discloses the use of this preparation method for the solid support of the europium-macrocyclic-complexes.

61. Also, it would also been obvious to one skilled in the art to utilize the solid support europium-macrocyclic-complexes of the combined disclosures for the method

Art Unit: 1618

for analysis of a sample suspected of containing at least one analyte as Leif et al. teaches that the combination of gadolinium (III) complex in the presence of other solutes to the difunctionalized macrocyclic molecules which were taught in Vallarino et al. US 5,696,240 (not excluding the solid support europium-macrocyclic-complexes) provides for enhanced luminescence and enable the detection and/or quantitation of many analytes in low concentrations without the use of expensive, complicated time-gated detection systems (Leif et al. abstract).

62. It is respectfully pointed out that instant claims 8,9 and 11-13 are product-by-process limitations. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed Cir. 1985). See MPEP 2113.

63. Also, the intended use, such as unitary luminescence enhancing solution is not generally afforded any patentable weight and since the combination leads to the same compounds as claimed, they would be expected to be capable of performing the same intended use. "The recitation of a new intended use for an old product does not make a claim to that old product patentable." *In re Schreiber*, 44 USPQ2d 1429 (Fed. Cir. 1997).

***Response to Arguments***

64. Applicant's arguments filed 8/9/10 have been fully considered but they are not persuasive.

65. Applicant asserts that the examiner addresses only claims 14 and 15 individually. Applicant takes the examiner's arguments not directed to those claims that apply generally to claims 1-13.

66. The office action mailed 2/8/10 states that Leif et al. (US 6,340,744 B1) discloses spectrofluorimetrically detectable luminescent compositions comprising a.) at least one energy transfer acceptor lanthanide element macrocycle compound which may be substituted with reactive functional groups at which reaction with analytes can take place ***as well as that stated above***. Therefore, all of the statements provided about the reference of Leif et al. in the preceding paragraphs are included in the rejection under 35 U.S.C. 103(a) and thus address the instant claims 8,9,11 and 12

67. Also, the office action states that Leif et al. further disclose the concentration range of the energy transfer donor species is in the range from  $1 \times 10^{-5}$  to  $1 \times 10^{-3}$  moles per liter (column 10, lines 4-8) which encompasses the concentration range of the energy transfer donor of the instant claims which addresses the instant claim 13.

68. The reference of Mathis et al. was used to teach of macropolycyclic rare earth complexes, namely cryptates which are useful as fluorescent tracers for biological substances in immunological detection or determination techniques using fluorescence to address the instant claim 18.

Art Unit: 1618

69. Applicant asserts that the reference of Mathis et al. does not disclose, suggest, use of a cryptate with the compounds of the present invention as part of an energy transfer acceptor lanthanide ion complex. The compounds disclosed by Mathis et al. and the chemistry of those compounds, is not the same as that of the present macrocyclic compounds. There is nothing in Mathis et al. that would lead one of ordinary skill in the art to substitute the cryptate of Mathis et al. for the macrocyclic chelator of the present invention.

70. Mathis et al. was not used to teach of the compounds of the instant claims but was used to teach that cryptates are useful as fluorescent tracers for biological substances in immunological detection or determination techniques using fluorescence. The excitation of the cryptate rare earth complexes enhances the fluorescence characteristics of a rare earth ion as excitation of an isolated rare earth ion produces only a very weak fluorescence because they generally have low molar absorption coefficients  $\epsilon$ .

71. At the time of the invention one ordinarily skilled in the art to substitute the cryptate of Mathis et al. for the macrocyclic chelator of Leif et al. to examine the enhancement of the fluorescence of the luminescent compositions for determination techniques as excitation of the cryptate rare earth complexes enhances the fluorescence characteristics of a rare earth ion which generally have low molar absorption coefficients  $\epsilon$ .

72. It is obvious to those skilled in the art to make known substitutions on compounds that are similar in structure and function to observe the effects on the

Art Unit: 1618

function of such compounds and to use the observations/data to further manipulate a compound to generate the desired effect, such as the enhancement of the fluorescence of the luminescent compositions for use in the detection and/or quantitation of many analytes in low concentration without the use of expensive, complicated time-gated detection systems.

73. Applicant asserts that with respect to claims 14 and 15, applicant notes that these claims require a unitary luminescence enhancing solution.

74. Leif et al. teaches of adding a luminescence-enhancing amount of at least one energy transfer donor compound which encompasses the unitary luminescence enhancing solution.

75. The intended use, such as unitary luminescence enhancing solution is not generally afforded any patentable weight and since the combination leads to the same compounds as claimed, they would be expected to be capable of performing the same intended use. "The recitation of a new intended use for an old product does not make a claim to that old product patentable." *In re Schreiber*, 44 USPQ2d 1429 (Fed. Cir. 1997).

### ***Previous Rejections***

### ***Response to Arguments***

76. Applicant's arguments filed 8/9/10 have been fully considered but they are not persuasive.



### ***Double Patenting***

77. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Art Unit: 1618

78. Claims 1,3 and 4 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 4 of U.S. Patent No. 5,696,240 and over claims 4,27 and 34 of U.S. Patent No. 5,373,093.

79. Applicant asserts that claim 1 has been amended to render the claim patentably distinct from the cited claims of U.S. Patent No. 5,696,240 U.S. Patent No. 5,373,093.

80. US 5,696,240 teaches that the M metal ion may be selected from an actinide having atomic number 89-103 and thus the fluorophore and lumiphore are not a ligand of yttrium or a 3-valent lanthanide element having atomic number 59-71.

81. US 5,373,093 teaches that the M metal ion may be selected from an actinide (actinide series) having atomic number 89-103 and thus the fluorophore and lumiphore are not a ligand of yttrium or a 3-valent lanthanide element having atomic number 59-71.

82. Claim 14 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,750,005.

83. Applicant asserts that with respect to claim 14, applicant disagrees with the Examiner's assessment relating to claim 1 of U.S. Patent No. 6,750,005 as claim 14 of the instant claims requires a unitary luminescence enhancing solution.

84. The intended use, such as unitary luminescence enhancing solution is not generally afforded any patentable weight and since the combination leads to the same compounds as claimed, they would be expected to be capable of performing the same

Art Unit: 1618

intended use. "The recitation of a new intended use for an old product does not make a claim to that old product patentable." *In re Schreiber*, 44 USPQ2d 1429 (Fed. Cir. 1997).

### ***Conclusion***

85. No claims are allowed at this time. Claim 10 is objected to for depending on a rejected base claim.

86. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

Art Unit: 1618

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/  
Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/  
Examiner, Art Unit 1618